

Online Research @ Cardiff

This is an Open Access document downloaded from ORCA, Cardiff University's institutional repository: <https://orca.cardiff.ac.uk/id/eprint/112037/>

This is the author's version of a work that was submitted to / accepted for publication.

Citation for final published version:

Moriconi, Chiara ORCID: <https://orcid.org/0000-0001-7942-2166>, Palmieri, Valentina, Tornillo, Giusy, Fillmore, Helen, Pilkington, Geoffrey J. and Gumbleton, Mark ORCID: <https://orcid.org/0000-0002-7386-311X> 2018. Caveolin-1, a driver of invasive phenotype in in-vitro 3D-spheroid assays comprised of high grade GBM cells association with an AKT-inhibited phenotype. Neuro-Oncology 20 (S1) , i13-i13. 10.1093/neuonc/nox238.058 file

Publishers page: <https://doi.org/10.1093/neuonc/nox238.058>
<<https://doi.org/10.1093/neuonc/nox238.058>>

Please note:

Changes made as a result of publishing processes such as copy-editing, formatting and page numbers may not be reflected in this version. For the definitive version of this publication, please refer to the published source. You are advised to consult the publisher's version if you wish to cite this paper.

This version is being made available in accordance with publisher policies.

See

<http://orca.cf.ac.uk/policies.html> for usage policies. Copyright and moral rights for publications made available in ORCA are retained by the copyright holders.



Caveolin-1, a driver of invasive phenotype in in-vitro 3D-spheroid assays comprised of high grade GBM cells association with an AKT-inhibited phenotype.

Chiara Moriconi (Cardiff University/ School of Pharmacy and Pharmaceutical Sciences)

Valentina Palmieri (National Research Council of Rome/institute of Complex Systems)

Giusy Tornillo (Cardiff University/European Cancer Stem Cell Research Institute)

Geoffrey Pilkington (University of Portsmouth/Brain Tumour Research Centre of Excellence)

Mark Gumbleton (Cardiff University/ School of Pharmacy and Pharmaceutical Sciences)

INTRODUCTION

Glioblastoma multiforme (GBM) cells display a highly invasive phenotype, a hallmark which counters effective surgical and radiotherapy strategies. Caveolin-1 (Cav-1) is the main structural and functional component of caveolae. The impact of the expression of Cav-1 within a range of tumour and tumour-associated stromal cells is variable with both oncogenic and tumour suppressive roles reported which appear to be both disease-specific and context-dependent. Our hypothesis is that Cav-1 serves as promoter of invasion of GBM cells.

MATERIALS AND METHODS

To investigate our hypothesis we used a lentiviral shRNA approach to silence Cav-1 in three GBM cell lines (U87, UP007, UP029) derived from adult brain tumours. We employed an in-vitro 3D cell-sprouting invasion assay with GBM cell spheres embedded in Matrigel. Quantification of invasion was undertaken using a novel image analysis tool or 3D systems, INSIDIA (ImageJ Macro for High-throughput Spheroid Invasion Analysis). Parallel migration and invasion studies were performed using a Boyden Chamber approach, as well as cell-cell adhesion assays. Activation of signalling pathways in 2D and 3D cultures were performed by proteomic array and Western Blot analysis.

RESULTS AND CONCLUSION

GBM cells expressing Cav-1 (Cav-1 +ve) displayed a higher invasive capacity compared cells where Cav-1 had been silenced (Cav-1 -ve), the latter also showing increased cell-cell adhesion. A significant finding from the signalling analysis was an inverse association between Cav-1 silencing and activation of AKT evidenced by increased phosphorylation at both Ser473 and Thr308 sites. Ongoing studies are exploring this signalling axis and its relationship to the invasive phenotype.

CM and MG acknowledge Cancer Research Wales support. GP and HF acknowledge Brain Tumour Research support.